

sensitivity measurements, fundus photography and measurements with Optical Coherence Tomography. Pupillary measurements were obtained twice using NeuroOptics® VIP™-200 Pupillometer at scotopic, low mesopic, high mesopic and photopic lighting conditions by trained observers. A time interval of 30 minutes was provided between two sets of measurements and subjects were allowed to dark adapt for 1-2 minutes prior to any measurements being performed.

Results: Figure 1 provides the pupillary measurements under various illumination conditions. The mean difference in pupillary measurements obtained at attempt 1 and attempt 2 were 0.42, 0.62, 0.79 and 0.73 for the scotopic, low mesopic, high mesopic and photopic conditions respectively which was significant (Paired samples t-test, $p < 0.001$ for all comparisons). The 95% limits of agreement of pupillary measurements is also given in figure 1 and are on average -1.99 to +0.70.

Conclusions: Small yet significant differences in pupil measurements can occur during repeat measurements which is in the range of half a millimeter when measuring with NeuroOptics® VIP™-200 Pupillometer. One should consider multiple measurements at different times and averaging the values if accurate pupil dimensions are needed.

Table 1
Agreement of pupillary measurements under various lighting conditions

Lighting condition	Attempt 1	Attempt 2	95% limits of Agreement
Scotopic*	6.01	5.58	-1.75 to + 0.91
Low mesopic*	5.87	5.25	-2.02 to + 0.78
High mesopic*	5.52	4.73	-2.36 to + 0.79
Photopic*	4.80	4.07	-1.84 to + 0.38

All measurements listed are in millimeters

*The pupillary measurements obtained in attempt 1 was significantly higher than measures obtained in attempt 2 ($p < 0.001$) under different lighting conditions.

Commercial Relationships: Cherell Lemons, None; Min Kong, None; Danica Quicho, None; Arlene Flores, None; Danielle Ringle, None; Katalina Rowland, None; Kaydee McCray, None; Jennifer Kurtz; Pinakin G. Davey, None

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Dependence of melanopsin-mediated human pupil responses upon light level and stimulus masking

Manuel Spitschan¹, Jack Ryan², David H. Brainard¹, Geoffrey K. Aguirre². ¹Department of Psychology, University of Pennsylvania, Philadelphia, PA; ²Department of Neurology, University of Pennsylvania, Philadelphia, PA.

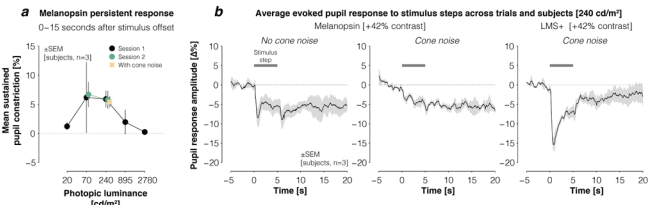
Purpose: We measured how signals from melanopsin (Mel) drive the human pupil response as a function of overall light level, and what components of the response are altered by stimulus masking.

Methods: We created Mel-directed light steps (method of silent substitution, +42% Mel contrast, nominally silent for the LMS cones). After removing residual luminance and chromatic stimulus components with psychophysical nulling, three observers viewed these steps (5.5 sec, 250 msec half-cosine window at on/offset) as modulations of a spatially uniform annular field (5° id, 27.5° od, CIE $x=0.50$, $y=0.40$) at five logarithmically-spaced photopic light levels. The viewing eye was pharmacologically dilated and consensual pupil responses were recorded in the other eye. Step onset time was jittered across the 45 second trials.

Results: At 70 and 240 cd/m², there was a sustained pupil constriction in response to the Mel-directed steps that persisted beyond step offset until the end of the trial. Repeat measurements at these light levels replicated the effect. The sustained response was not clearly different from zero at 20, 895, and 2780 cd/m². At all

light levels, there was also a transient pupil constriction at both onset and offset of the Mel-directed step. To address the possibility that the observed responses were in fact due to residual stimulation of the cones and/or awareness of the stimulus, the measurements were repeated at 240 cd/m² with added cone noise (8 Hz noise uniformly distributed between $\pm 3\%$ L+M+S and $\pm 3\%$ L–M contrast). This noise masked the visibility of the Mel-directed steps, but not that of control L+M+S cone-directed steps (+42% contrast). This manipulation greatly reduced the transient responses to the Mel-directed steps, but left the sustained response unaltered. Transient responses, however, remained for the L+M+S cone-directed steps, despite the noise.

Conclusions: Mel-directed contrast steps presented on mid-photopic backgrounds evoke sustained pupil responses even when masked by cone noise. The magnitude of sustained response depends strongly on background light level, with maximal response observed at 70 and 240 cd/m². This dependence could be due to properties of the melanopsin-containing retinal ganglion cells and/or to the properties of the pupil control system.



a) Time average pupil responses as a function of light level in three subjects; b) Average pupil time series at 240 cd/m².

Commercial Relationships: Manuel Spitschan; Jack Ryan, None; David H. Brainard, U.S. Patent Application No. 14/852,001 (P); Geoffrey K. Aguirre, U.S. Patent Application No. 14/852,001 (P) **Support:** NIH Grant EY024681, NIH Grant EY020516, DoD Grant W81XWH-15-1-0447, NIH Grant P30 EY001583

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Smartphone-based Head-mounted Binocular High-Speed Pupillometer

Wolfgang Fink^{1,2}, Kevin Garcia³, Mark Tarbell^{1,2}. ¹Dept. of Biomedical Engineering, University of Arizona, Tucson, AZ; ²Visual and Autonomous Exploration Systems Research Laboratory, Caltech, Pasadena, CA; ³Breault Research Organization, Inc., Tucson, AZ.

Purpose: (1) In general, to provide ophthalmic healthcare to people who live/operate in austere environments (e.g., third world, natural disaster areas, military environments), or are geographically dispersed (e.g., rural populations), where time, cost, and impossibility of travel make access to even adequate medical care difficult if not impossible. (2) In particular, to provide a head-mounted binocular high-speed pupillometer.

Methods: Optical add-on adaptors, specifically designed for a variety of ophthalmic metrology applications, are developed that act as ophthalmic examination extensions to a smartphone. A healthcare practitioner attaches such a device to a smartphone and runs a custom app to perform a specialized examination of specific areas of the eye. The smartphone app submits the collected examination data through a wireless connection to a server-backend for medical analysis. The analysis results are sent back in near real-time and are displayed onscreen to the on-site practitioner to facilitate, e.g., a triage process.

Results: A smart service platform in ophthalmology was devised by creating a server-based telediagnostic analysis capability for current and future smartphone-based ophthalmic examination devices. The first such ophthalmic examination device developed

is a head-mounted, miniaturized pupillometer, composed of an optical add-on adapter coupled to a smartphone, that allows for the simultaneous recording of pupillary behavior of both eyes at 120Hz in the presence and absence of light stimulation, i.e., pupillary light reflex and dark reaction. Examination data gathered are sent via Wi-Fi or cell signal through a smartphone app to a server for automated video analysis. Analysis results, including the pupillary diameter displayed as a function of time for each eye in addition to parameters such as pupillary latency, constriction, and dilation times, are sent back to the originating smartphone in near real-time for further assessment by the on-site practitioner.

Conclusions: In general, the new paradigm of *Smart Ophthalmics*, i.e., smart tele-ophthalmology, may greatly improve remote patient screening and triage, and help ensure that undiagnosed eye diseases are detected early and treated in time to prevent permanent vision impairment. In particular, the binocular pupillometer enables performing the swinging flashlight test, and may allow the diagnosis of afferent and efferent pupillary defects.

Commercial Relationships: Wolfgang Fink, University of Arizona (P), Caltech (P); Kevin Garcia; Mark Tarbell, University of Arizona (P) **Support:** NSF Award #IIP-1430062

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Presentation Time: 8:30 AM–10:15 AM

Effect of induced glare on pupil size in ocular healthy adults

Arlene Flores¹, Danica Quicho¹, Min Kong², Cherell Lemons¹, Katalina Rowland², Danielle Ringle², Kaydee McCray², Jennifer Kurtz², Pinakin G. Davey^{2,1}. ¹Graduate College of Biomedical Sciences, Western University of Health Sciences, Pomona, CA; ²College of Optometry, Western University of Health Sciences, Pomona, CA.

Purpose: Glare testing in clinical setting is complicated due to the lack of clear gold standard. This becomes particularly important when evaluating for cataract surgery where decisions are made on the basis of changes in visual performance with glare. We sought to investigate two calibrated glare inducing systems and evaluate the change in pupil size when the light levels were standardized.

Methods: One hundred eyes of 50 individuals in age range 20 to 35 were included in the study. Subjects underwent an ocular health examination that included vision testing, fundus photography and measurements with Optical Coherence Tomography. The glare units were placed at 8 feet viewing distance from the subject. The glare system 1 (GS1) involves LED light illumination and is constructed with four LED lights at four corners of the monitor. The glare system 2 is a retro illuminated chart with two halogen lamps placed at either side of the box. The background illumination of GS1 and GS 2 system measured at 1 foot was 3 and 25 lux. With the glare levels turned on both units were set at 48 lux. Pupillary measurements were obtained twice using NeuroOptics® VIP™-200 with glare system off and glare system turned on.

Results: Figure 1 provides the pupil size with and without induced glare. The baseline pupil measurements when inducing glare GS1 LED system had pupil size of 5.93 which decreased to 4.01 mm with glare. The baseline pupil measurements when inducing glare GS2 halogen system had pupil size of 5.46 which decreased to 3.96 mm with glare. The change in pupil size was significant with both glare systems (Paired samples t-test $t=23.77$; $p<0.001$ and $t=23.41$; $p<0.001$). The pupil measurements without the glare lights on was different when using the GS1 versus GS2 with pupil 0.47 mm larger when using GS1 (Independent samples t-test $t=7.29$; $p<0.001$). The pupil size was not significantly different when the glare lights were turned on (Independent samples t-test $t=1.12$; $p=0.26$).

Conclusions: Difference in background illumination of glare systems caused a measurable difference in pupil size at baseline. The calibration of glare systems is an important factor in predicting the outcome of visual performance and should be considered when using different glare units. The pupil size is not affected by the glare source; LED versus Halogen.

Table 1

Pupil measurements using with and without glare

Glare system	Pupil size without glare	Pupil size with glare	Difference
GS1 (LED based system)	5.93	4.01	1.92
GS2 (Halogen light based system)	5.46	3.95	1.52

Pupil size in mm

Light levels of glare induced was 48 lux for both Glare system 1 (GS1) and Glare system 2 (GS2).

Commercial Relationships: Arlene Flores, None; Danica Quicho, None; Min Kong, None; Cherell Lemons, None; Katalina Rowland, None; Danielle Ringle, None; Kaydee McCray, None; Jennifer Kurtz, None; Pinakin G. Davey, M&S Systems (C)

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Interactions between photic drive responses and multifocal pupillography in epilepsy

Ted Maddess¹, Eman N. Ali¹, Corinne F. Carle¹, Andrew C. James¹, Kate Martin², Angela Borbely², Christian J. Lueck^{2,1}. ¹Neuroscience, Australian National University, Canberra, ACT, Australia; ²Neurology, The Canberra Hospital, Canberra, ACT, Australia.

Purpose: Photic drive responses (PDRs) have been used to explore cortical hyper-excitability in neurological disorders. We quantified changes PDR in epilepsy patients and looked for interactions with responses obtained from multifocal objective pupillographic perimetry (mfPOP).

Methods: This was a cross-sectional study of 15 consecutive epilepsy patients (8 males; mean age \pm SD 47.3 ± 4.6 years), and 15 controls (9 males; mean age 52.7 ± 4.6 years) undergoing routine EEG with standard intermittent photic stimulation (IPS) and testing with the mfPOP device. EEG spectral amplitudes during IPS were obtained using the Fourier transform. N-fold changes in PDR (expressed in dB) when IPS and alpha bands overlapped, the alpha-band gain, were examined and also their interaction with mfPOP responses. Alpha-band gain was determined by comparing eyes-open and eyes-closed conditions. mfPOP responses were obtained from 44 regions/visual field. Response time-to-peak and standardized amplitude was recorded for each test region.

Results: A linear model showed that an epileptic attack within 1 month increased the alpha-band gain by 1.33 dB ($p=0.01$). Generalised epilepsy (i.e. no focal epilepsy) decreased the alpha-band gain by 1.03 dB ($p=0.03$). For each decade increase in age the gain increased by 0.36 dB ($p=0.007$). For every 1 dB increase in alpha band gain pupil responses were reduced by 0.207 ± 0.09 dB on average across the field ($p=0.024$).

Conclusions: Investigating alpha-band gain offers another way to quantify cortical hyper-excitability in epilepsy patients. Responses to mfPOP may provide less invasive means to quantify hyper-excitability.

Commercial Relationships: Ted Maddess, EyeCo Pty Ltd (I), nuCoria Pty Ltd (P), nuCoria Pty Ltd (F), nuCoria Pty Ltd (I); Eman N. Ali, None; Corinne F. Carle, nuCoria Pty Ltd (F), nuCoria Pty Ltd (P), nuCoria Pty Ltd (I); Andrew C. James, nuCoria Pty Ltd